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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,590	07/29/2003	Peter S. Lu	VITA-008	4993

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/630,590	LU ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 10-20* is/are pending in the application.

4a) Of the above claim(s) *16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8 and 10-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1, 3-8, and 10-20 are pending. In the prior action, mailed on February 16, 2005, claims 1-15 were under consideration and rejected, and claims 16-20 were withdrawn as to nonelected inventions. In the Response filed on July 18, 2005, the Applicant amended claims 1, 3, 6, and 10; and cancelled claims 2 and 9. Claims 1, 3-8, and 10-15 are under consideration.

Priority

2. In the prior action, it was noted that the Applicant had not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 to prior application 09/710,059. The Applicant has cancelled reference to this application in the specification and in the Application Data Sheet.

Specification

3. **(Prior Objection- Withdrawn)** The specification was objected to as failing to provide proper antecedent basis for methods of using PDZ domain polypeptides that bind E6 proteins encoded by HPV strains 16, 18, and 45. In view of the amendment to the specification, the objection is withdrawn.

Claim Objections

4. **(Prior Objection- Objection)** Claims 1, 7, and 10 were objected to because of the following informalities: each of these claims refer to the human papillomavirus in the first instance as HPV, without first identifying the virus by its complete name. In view of the amendment of the claims, the objection is withdrawn.

5. **(Prior Objection- Objection)** Claim 3 was objected to because of the following informalities: the claim provides a list of HPV strains in line 2. It was suggested that a comma be inserted between the last two members of the list so that the claim identifies strains - - 16, 18, and 45- -. In view of the amendment of the claims, the objection is withdrawn.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. **(Prior Rejection- Withdrawn)** Claims 1, and 3-15 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of detecting the presence of an oncogenic HPV by contacting a sample with the Magi-I PDZ domain 2, does not reasonably provide enablement for methods of using any PDZ domain polypeptide for the detection of any oncogenic HPV or HPV E6 protein in the sample. In view of the amendment of the claims such that the claims now require that the PDZ domain polypeptide comprises PDZ domain 2 of MAGI-1, the rejection is withdrawn.

8. **(Prior Rejection- Withdrawn)** Claims 1, 3-8, 10-15 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement with respect to methods of using any PDZ domain in the detection of oncogenic HPV E6 proteins. In view of the amendment of the claims requiring the use of PDZ domain 2 of MAGI-1, the rejection is withdrawn.

9. **(Prior Rejection- Withdrawn)** Claim 3 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement with respect to the use of any PDZ domain polypeptide falling within the genus of PDZ domain polypeptides that bind the E6 proteins of each of HPV strains 16, 18, and 45. In view of the amendment of the claims requiring the use of PDZ domain 2 of MAGI-1, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. **(Prior Rejection- Withdrawn)** Claims 1, 4-8, 10-13, and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Davis et al. (U.S. 5610,077- of record in the May 2004 IDS) in view of Bleul et al. (U.S. 5,753,233- of record in the September 2003 IDS) and either of Kiyono et al. (PNAS 94: 11612-16) or Gardiol et al. (Oncogene 18: 5487-96- of record in the May 2004 IDS). In view of the amendment of the claims to require that the PDZ domain is the second PDZ domain of MAGI-1, the rejection is withdrawn.

12. **(Prior Rejection- Withdrawn)** Claims 1, 4-8, 10-13, and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Davis in view of Bleul and Lee et al. (PNAS 94: 6670-75- of record in the September 2003 IDS). The claims have been described above, as have the teachings of both Davis and Bleul. In view of the amendment of the claims to require that the PDZ domain is the second PDZ domain of MAGI-1, the rejection is withdrawn.

13. **(Prior Rejection- Maintained)** Claims 1-13, and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Davis in view of Glaunsinger et al. (Oncogene 19: 5270-80) and Bleul. The claims are drawn to methods of detecting infection by oncogenic HPV, or the E6 proteins of such virus, by contacting a sample suspected of containing such a molecule with 1) a PDZ domain polypeptide that comprises the Magi-I PDZ domain 2 sequence, and (optionally) 2) an antibody that binds to the E6 protein. The rejection is withdrawn from claims 2 and 9, which have been cancelled from the application.

The Applicant traverses the rejection on three grounds. First, the Applicant argue that there is no suggestion in the prior art references that a PDZ domain of MAGI-1 could specifically bind to the E6 proteins of all known oncogenic E6 proteins. Second, the Applicant argues that the Glaunsinger reference teaches away from the claimed invention in that the reference teaches that the MAGI-1 protein would be degraded in performing the test. The Applicant's third argument is that the present claims recite that the PDZ domain used comprises the second PDZ domain of MAGI-1, whereas Glaunsinger teaches a protein that is a full length MAGI-1. These arguments are not found persuasive.

The teachings of the three references have been described previously. As indicated in the prior action, Davis teaches methods for the detection of analytes comprising two binding partners to an intended analyte. Although the reference indicates that the binding partner in the preferred embodiments are antibodies, the teachings of the patent would have rendered it obvious to those in the art that any binding partner to the intended analyte may be used. Bleul teaches the

diagnosis of HPV, or the detection of HPV polypeptides in a sample, through use of antibodies directed against the HPV E6 protein. From these teachings, it would also have been obvious that a second binding partner for the HPV E6 protein could be used in a method such as that disclosed in Davis, which requires the use of two binding partners.

Glaunsinger identifies the Magi-I protein as a PDZ polypeptide which is bound by the oncogenic HPV E6 proteins. Thus, it would have been apparent to those in the art that this protein could act as a second binding partner for at least the oncogenic E6 proteins of at least oncogenic strains 16 and 18 of HPV. Further, the reference teaches that the MAGI-1 protein is not able to bind to the E6 proteins of non-oncogenic HPV-11. Thus, it would have been obvious to those in the art that the MAGI-1 protein disclosed in the reference could be used in the detection of oncogenic HPV –16 and –18 E6 proteins, especially where used in combination with antibodies specific to these proteins.

As indicated above, the Applicant argues that the teachings of these references do not render the claims obvious because they do not teach that MAGI-1 could bind to any oncogenic HPV. However, regardless of whether the reference would have rendered it obvious to detect all oncogenic E6 proteins, the reference renders at least the detection of HPV strains 16 and 18 obvious. The fact that these two species of the claimed genus are rendered obvious is sufficient to render the claim as a whole obvious.

The Applicant's second argument is that the additional teachings of Glaunsinger teach away from the use of the MAGI-1 protein for the detection of oncogenic E6 proteins because the reference teaches that the MAGI-1 proteins are degraded in the presence of the viral proteins.

The Applicant argues that this teaching makes the MAGI-1 protein unsuitable for use in the claimed method. This argument is not found persuasive for two reasons. Both of these reasons are based on the cited teachings of the Glaunsinger reference which states on page 5278 that "high-risk HPV E6 proteins target MAGI-1 for degradation *in cells*" (emphasis added). This statement provides two elements relevant to the Applicant's argument. First, the statement teaches that the degradation occurs in cells. Second, the statement teaches that the E6 proteins do not themselves degrade MAGI-1, but, in combination with the prior teaching, indicate that the E6 proteins target it for degradation by other cellular mechanisms. Thus, while E6 binding to MAGI-1 would result in degradation of the protein within a cell, such would not be the case in an in vitro assay. This is demonstrated by the use of such a binding assay to determine if the E6 and MAGI-1 proteins bind as seen in Figure 8, and on page 5277 (the carryover paragraph from page 5276). For these reasons, the Applicant's second argument is not found persuasive.

The Applicant's third argument is that the teachings of Glaunsinger fail to appreciate that the binding of the oncogenic E6 proteins specifically to the second PDZ domain of MAGI-1, and that the reference teaches the use of a full length MAGI-1, and not only the second PDZ domain. This argument is not found persuasive because, while the claims require the presence of the second PDZ domain of MAGI-1 (which would be inherently present in that of the full length protein) the claims do not exclude the use of the full-length protein. Thus, the Applicant appears to be asserting that the reference does not meet the limitations of the present claim because the reference does not teach the use of a peptide comprising only the second PDZ domain of MAGI-1, a limitation which is not found in the claim. Because the claims are not limited to the use of

PDZ polypeptides consisting of the sequence of the second PDZ domain of MAGI-1, the argument is not found persuasive.

For these reasons, and for the reasons of record, the rejection is maintained against pending claims 1, 3-8, 10-13, and 15.

14. **(Prior Rejection- Maintained)** Claim 14 was rejected under 35 U.S.C. 103(a) as being unpatentable over Davis in view of Bleul and Glaunsinger as applied above, and further in view of Kehmeier et al. (Virology 299: 72-87). The Applicant traverses this rejection on the same grounds as asserted with respect to pending claims 1, 3-8, 10-13, and 15 above. These arguments were not found persuasive for the reasons provided. Because the Applicant provides no addition arguments in traversal of this rejection, it is maintained for the reasons above, and the reasons of record.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. **(Prior Rejection-Maintained)** Claims 1-15 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 8, 9, 10 of copending Application No. 10/847,818. The Applicant traverses the rejection on the basis that the claims of the copending application do not teach or suggest the presently claimed inventions. However, while this may be the case, the Office is permitted to look to the specification of the application to determine the meaning and scope of the claims of the copending application. As was indicated in the prior action, the examples provided in the application illustrate that the claims of that application read on the presently rejected claims, and that based on the disclosure of the application describing embodiments of the claimed invention, the present claims represent an obvious variation on the copending claims. The rejection is therefore maintained.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

17. No claims are allowed.

18. The following prior art reference was made of record in the prior action. Thomas et al., Oncogene, 20: 5431-39. It is noted that this reference teaches that the first, rather than the second, PDZ domain of MAGI-1 is bound by the HPV E6 proteins. Page 5437. However, the reference also teaches that this domain corresponds to a region around residues 454-582 of the MAGI-1 sequence. Page 5438, left column. A comparison of SEQ ID NO: 288 (identified as the PDZ2 domain of MAGI-1 on page 120, Table 9, the application) with that of resides 454-582 of

GenPept Accession AAB91995 shows that the two sequences are overlapping. Thus, the PDZ1 domain of the reference Thomas corresponds to the PDZ2 domain of the present application. The teachings of this reference would therefore render obvious the claims if limited to polypeptide comprising only the second PDZ domain of MAGI-1.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 8/8/05
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